REMARKS

The instant Amendment B is responsive to the Office Action dated February 12, 2004. Applicant respectfully submits that claims 1-13, 17-19, and 21-23 as set forth herein patentably distinguish over the cited references, and respectfully request allowance of all claims as set forth herein.

The current status of the claims

The previously indicated allowability of claims 3-8, 12, 15, 16, 18, and 20-23 has been withdrawn in the Feb. 12th Office Action in view of newly discovered references Loncar et al. 6,075,362 (hereinafter "Loncar"), Ericcson et al. 5,869,023 (hereinafter "Ericcson"), and Rocklage et al. 5,190,744 (hereinafter "Rocklage"). Specifically:

Claims 1-7, 9-11, 13, and 15-21 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Loncar in view of either Rocklage or Ericcson.

Claim 8 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Loncar in view of either Rocklage or Ericcson, in further view of Foxall 6,492,811 (hereinafter "Foxall").

Claims 12, 22, and 23 stand rejected under 35 U.S.C. §102(e) as being anticipated by Loncar in view of either Rocklage or Ericcson in further view of Wang 6,650,925 (hereinafter "Wang").

As these are new grounds of rejection, the Feb. 12th Office Action is non-final.

The Loncar reference

Loncar is primarily directed toward a dual contrast imaging approach in which readout of k-space lines of the two images having different contrast weightings are interleaved. Loncar describes in the Background section the approach of acquiring the two images sequentially during the spin echo imaging sequence (col. 1 lines 37-45). Applicants also describe this sequential dual contrast approach in the Background of the Invention of the present application (page 3 lines 15-21).

Loncar does not disclose acquiring non-T_2 imaging data during the deadtime extending between the initial RF excitation pulse and the RF inversion or refocusing pulse that creates the spin echo. Loncar does not disclose a sequence of the type shown in FIGURE 3 of the present application, for example, in which non-T_2 weighted data, such as T_1 or T_2^* weighted data, are acquired between the RF excitation pulse **200** and the RF inversion pulse **212**.

This deadtime is substantial; indeed, it is equal to the time between the refocusing pulse and the maximum amplitude of the spin echo produced by the refocusing pulse. The present application, unlike Loncar, recognizes that this deadtime can be used for acquiring the second image of the dual contrast imaging sequence.

Moreover, the Office Action acknowledges at page 3 that Loncar does not disclose or fairly suggest employing dual or multiple contrast imaging in conjunction with contrast enhanced imaging. Indeed, Loncar nowhere mentions administering any contrast agent. Rather, the Office Action asserts that Loncar in combination with either of Rocklage or Ericcson renders obvious this aspect of the present application.

The Rocklage and Ericcson references

Rocklage and Ericcson are directed toward contrast enhanced magnetic resonance imaging techniques, in which a magnetic contrast agent is administered to the imaging subject prior to acquiring imaging data. The magnetic contrast agent shows up in the magnetic resonance images, allowing the imaging to locate and track the contrast agent in the subject. Applicants also describe such existing contrast enhanced imaging techniques in the Background of the Invention of the present application (page 3 lines 22 ff).

The Office Action's proposed combination of either of either Rocklage or Ericcson with Loncar ignores the fact that there is no motivation in any of these references to make such a combination. The two techniques of dual contrast imaging and contrast enhanced imaging are two entirely different ways of accomplishing the same result, namely obtaining improved image contrast. Their combination would appear on its face to be redundant.

Rocklage recognizes (col. 6 lines 52-62) that a contrast agent such as Gd(III) provides both T_1 and T_2 contrast. However, Rocklage strongly implies (col. 6 lines 62-68) that any approach combining T_1-contrast images and T_2-contrast images would be unsafe, and elsewhere (col. 4 lines 62-68) states that contrast agents providing negligible T_1 contrast are preferred over contrast agents such as Gd-based agents which provide a significant T_1 contrast. Taken as a whole, one skilled in the art would likely be motivated by Rocklage to avoid a contrast agent such as Gd(III) that provides both T_1 and T_2 contrast.

Claim 2 has been placed into independent form with additional elements, and patentably distinguishes over the cited references

Claim 2 has been placed into independent form, and calls for administering a contrast agent which alters T_1 and T_2 magnetic resonance characteristics, and exciting magnetic resonance in a region of interest. A first EPI waveform is applied generating first image data having T_1 contrast. A refocusing RF inversion pulse is applied after the first EPI waveform. A second EPI waveform is applied generating second image data having T_2 contrast and some T_1 contrast. The first image data are reconstructed into a first reconstructed image having T_1 contrast. The second image data are reconstructed into a second reconstructed image having both T_1 and T_2 contrast. The second reconstructed image is corrected based on the first reconstructed image to reduce the T_1 contrast of the second reconstructed image.

Claim 2 uses time prior to application of the refocusing RF inversion pulse for acquiring first EPI image data having T_1 contrast. Loncar does not suggest using this time for acquiring T_1 weighted data; rather, Loncar discloses acquiring both the T_1 weighted data and the T_2 weighted data during the spin echo, that is, after the refocusing pulse that generates the spin echo.

Claim 2 combines: (i) a dual contrast EPI imaging sequence which acquires T_1 weighted data prior to refocusing with (ii) the use of a contrast agent which alters T_1 and T_2 magnetic resonance characteristics. There is no motivation in the references, alone or in combination, to make this combination called for in claim 2. Because perfusion of the contrast agent in the

imaging subject may be rapid, imposing harsh time constraints on acquisition of T_1 and T_2 or T_2^* weighted data, it is not obvious that time-intensive dual contrast imaging techniques are combinable with contrast agent enhanced imaging. The method of claim 2 recognizes this problem, and solves it by (i) employing rapid EPI imaging; and (ii) acquiring T_1 weighted data in the time interval before refocusing, which is otherwise wasted.

Rocklage and Ericcson disclose contrast agents having T_1 and T_2 contrast effects, but do not suggest using such a contrast agent in conjunction with dual contrast imaging. Indeed, Rocklage teaches away from employing <u>any</u> contrast agent having a significant T_1 contrast, preferring instead (col. 4 lines 62-68) to use a contrast agent that has negligible T_1 contrast.

Accordingly, Applicants respectfully request allowance of claim 2 as set forth herein.

<u>Applicants ask for reconsideration of claims 1, 3-5, 9-11, 17 and 18 as set forth herein</u>

Claim 1 calls for administering a magnetic resonance contrast agent, applying a first echo planar readout waveform to generate first image data, applying a second echo planar readout waveform after the first echo planar readout waveform to generate T_2 or T_2^* weighted image data, reconstructing the image data to generate a first image representation and a T_2 or T_2^* weighted image representation, and correcting the T_2 or T_2^* weighted image representation with the first image representation.

Claim 1 stands rejected based on a combination of Loncar, which discloses dual contrast imaging, in combination with either Rocklage or Ericcson, both of

which disclose contrast enhanced imaging. However, none of these references, either alone or in tandem, provide any motivation to make the proposed combination.

The dual contrast imaging of Loncar provides one approach for achieving improved contrast. The contrast enhanced imaging of Rocklage and Ericcson provides another, different approach for achieving improved contrast. One skilled in the art would not be motivated by these references to combine these techniques.

Rocklage, recognizes (col. 6 lines 52-68) that some contrast agents provide both T_1 and T_2 imaging contrasts. However, Rocklage expresses substantial safety concerns regarding the use of both T_1 and T_2 contrasts in imaging such contrast agents. Instead, Rocklage strongly urges (col. 4 lines 62-68) that contrast agents providing negligible T_1 contrast be employed. One skilled in the art would not be motivated by Rocklage to combine dual contrast imaging with a contrast agent.

The present applicants have recognized that a gadolinium-based contrast agent, for example, makes T_2 images darker, but makes T_1 images brighter. Thus, in T_2 imaging, the T_1 decay that continues into the T_2 weighted imaging period counteracts the darkening effect of the contrast agent creating an error component in the T_2 image. Moreover, because the T_1 brightening decreases with time, the T_1 error is non-constant across the T_2 weighted data. The present inventors have found that in the time before T_2 image data collection commences, they can collect enough T_1 data to correct the T_1 brightening errors in the T_2 image data.

Unlike the references, the present application recognizes that: (i) dual contrast imaging can be used to

correct the contrast enhanced image for T_1 shortening or other non-T_2 effects; and (ii) EPI is sufficiently rapid to enable dual contrast imaging in conjunction with contrast enhanced imaging. The combination of dual contrast EPI imaging with a contrast agent is neither disclosed nor fairly suggested by the references.

Regarding **claims 9 and 10,** while Loncar discloses producing a third image, Loncar does not disclose producing a temporal series of third images depicting a temporal evolution of the contrast agent in the region of interest. Indeed, as acknowledged in the Office Action, Loncar does not address contrast enhanced imaging in any form whatsoever. Rocklage and Ericcson cannot remedy this deficiency of Loncar, because those references also do not disclose or fairly suggest producing from dual contrasts a temporal series of third images depicting a temporal evolution of the contrast agent.

Claim 11 calls for a gadolinium chelate as the contrast agent. Rocklage specifically teaches away from using a gadolinium-based contrast agent, preferring instead (col. 4 lines 62-68) to use a contrast agent such as a Dy-based contrast agent having a negligible T_1 contrast.

Accordingly, Applicants respectfully ask for reconsideration and allowance of claims 1, 3-5, 9-11, 17, and 18 as set forth herein.

Claims 6-8 as set forth herein patentably distinguish over the cited references

Claim 6 calls for administering a magnetic resonance contrast agent which alters T_1, T_2 and T_2^* magnetic resonance characteristics, exciting magnetic resonance applying a first echo planar readout waveform and generating first image data, and applying a second echo planar readout waveform and generating T_2 or T_2^* weighted image data. A T_2 or T_2^* weighted image representation is generated by reconstructing (i) the T_2 or T_2^* weighted image data and (ii) a portion of the first image data temporally adjacent to the T_2 or T_2^* weighted image data. A first image representation is generated by reconstructing (i) a portion of the T_2 or T_2^* weighted image data temporally adjacent to the first image data and (ii) the first image data. The T_2 or T_2^* weighted image representation is corrected with the first image representation.

Loncar discloses a dual contrast EPI imaging method in which k-space lines of the first and second images are interleaved throughout each echo. Optionally, some k-space lines may be shared between the images. However, Loncar does not disclose having the k-space lines of the two images temporally segregated into first and second EPI waveforms with sharing of only k-space lines at the adjacency between the two waveforms. Such an approach would defeat the advantages of Loncar's interleaving of the k-space lines of the first and second images.

However, sharing k-space lines at the adjacency is advantageous in the present application because it further speeds up acquisition of the dual contrast

imaging data in the context of a rapidly moving contrast agent bolus. Loncar does not use a contrast agent.

Accordingly, Applicants respectfully request allowance of claims 6-8 as set forth herein.

Claim 12 as set forth herein patentably distinguishes over the cited references

Claim 12 as set forth herein calls for administering a magnetic resonance contrast agent which alters T_1, T_2 and T_2^* magnetic resonance characteristics, exciting magnetic resonance by applying a radio frequency excitation pulse and subsequently applying a refocusing inversion pulse. A first echo planar readout waveform is applied during a deadtime between the radio frequency excitation pulse and the refocusing pulse. A second echo planar readout waveform is applied after the applying of the refocusing pulse.

Loncar does not disclose the EPI acquisition sequence called for in claim 12, in which the dead time between the RF excitation and RF refocusing is used to acquire a first echo planar readout waveform. Moreover, Loncar does not disclose the combination of dual contrast EPI and contrast enhanced imaging called for in claim 12. Neither Rocklage nor Ericcson can remedy these deficiencies of Loncar, because they also do not disclose or fairly suggest the dual contrast EPI sequence called for in claim 12.

Accordingly, Applicants respectfully request allowance of claim 12 as set forth herein.

Claim 13 as set forth herein patentably distinguishes over the cited references

Claim 13 recognizes that contrast agents can affect T_1 and T_2 or T_2^* decay characteristics. T_1 decay occurs exponentially decreasing faster than T_2 decay. T_2 data is typically collected after the T_1 effects have decayed to a level that the T_2 effects dominate. However, T_1 effects are typically still present. With a contrast agent such as gadolinium where the effects on T_1 and T_2 decay counteract, the effect of the contrast agent on the residual T_1 decay interferes with the interpreting of the T_2 or T_2^* weighted images. (Even when the effect is different, but not counteracting, the T_2 or T_2^* image interpretation can be impaired).

None of Loncar, Ericcson, or Rocklage recognize this problem, much less suggest that it can be cured through a variation on dual contrast imaging. Because none of the references recognize the problem, much less solve it, it is submitted that claim 13 distinguishes patentably and unobviously over the references of record.

Claim 19 and 21-23 as set forth herein patentably distinguish over the cited references

Claim 19 calls for a magnetic resonance imaging apparatus including a sequence controller which induces resonance including spin refocusing using an inversion RF pulse, generates EPI non-T_2 weighted data lines during a deadtime preceding the inversion RF pulse, generates EPI T_2 weighted data lines after the inversion RF pulse, and sorts the non-T_2 and T_2 weighted data lines. A reconstruction processor reconstructs data lines from the first data memory into a first image representation and

data lines from the second data memory into a second image representation.

Loncar does not disclose the sequence of claim 19 including generating EPI non-T_2 weighted data during a deadtime preceding the spin refocusing RF inversion pulse. Rather, Loncar discloses (col. 1 lines 38-45) acquiring all data during the spin echo, that is, after the refocusing RF inversion pulse. This deficiency is not remedied by Rocklage or Ericcson, which disclose the alternative contrast technique of using a magnetic contrast agent to produce magnetic contrast.

Accordingly, Applicants respectfully request allowance of claim 19 and 21-23 as set forth herein.

CONCLUSION

For the reasons set forth above, it is submitted that claims 1-13, 17-19, and 21-23 as set forth herein patentably distinguish over the references of record. Accordingly, allowance of claims 1-13, 17-19, and 21-23 as set forth herein is earnestly solicited.

Respectfully submitted,
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